Choice of Treatment Regimen for TB Infection

Most patients with TB infection should be treated

Because testing of persons at low risk of TB infection should not be done, persons that test positive for TB infection should generally be treated once active TB disease has been excluded with a chest radiograph and, if indicated, sputum smears, cultures, and nucleic acid amplification testing. However, some persons at low risk for TB infection are tested. Clinicians should not be compelled to treat low risk persons with a positive test for TB infection as the rate of false positive tests in such populations increases.

Emphasis on short course treatment of TB infection

Shorter regimens of 3 to 4 months for treating TB infection have been shown to be more likely to be completed and use of these shorter regimens is preferred in most patients. Drug-drug interactions and exposure to drug-resistant TB are frequent reasons these regimens cannot be used.

Shorter duration TB infection treatment regimens

Preference	Medication	Frequency	Duration
1	INH + rifapentine	Weekly	3 months
2	Rifampin	Daily	4 months
3	INH + rifampin	Daily	3 months
3	INH	Daily	6-9 months

12-dose weekly regimen of Isoniazid (INH) + rifapentine

- A preferred regimen with efficacy similar to 9 months of INH
- Recommended for adults and children 2 years and older
- Completion rates much higher than with 9 months of INH, up to 85-90%
- Several fold lower risk of hepatotoxicity than with 9 months of INH
- Initially studied and recommended using directly observed therapy (DOT); however, self-administered therapy (SAT) is an approved option as studies have found similar rates of completion compared to DOT in U.S. patients
- Hypersensitivity syndrome (fevers, flu-like symptoms, pre-syncope/syncope, hypotension) observed in some patients
- Reactions typically mild and most patients able to continue with regimen

Rifampin for 4 months

- Another preferred regimen if 12-dose regimen cannot be used
- Completion rates are higher than with INH
- 4 months of rifampin found to be noninferior compared to 9 months of INH
- Lower rate of treatment discontinuation due to adverse effects compared to INH
- Substantially (several fold) less hepatotoxicity than with INH
- Drug interactions are the major contraindications to use
- Rifabutin is a commonly used alternative with a significantly lesser degree of drug interactions

Isoniazid (INH) + rifampin for 3 months

- Recommended for adults and children of all ages
- Similar risk of TB disease, hepatotoxicity, and adverse events compared to INH for 6 months or greater
- May be greater risk of hepatotoxicity compared to using INH or rifampin alone
- Drug interactions with rifampin remain major contraindication to use

Isoniazid (INH) for 6 or 9 months

- Has low completion rates, often less than 50%
- Risk of hepatotoxicity is higher with INH than with rifampin or the 12-dose regimen of INH + rifapentine
- There is a large body of evidence supporting its effectiveness if taken to completion
- INH should be considered when patients have significant drug-drug interactions with rifamycins
- Should be used with caution in patients with significant baseline liver disease
- Has significant interactions with anticonvulsant medications including phenytoin, carbamazepine and valproic acid

Children

- Ensuring that children, particularly those under 5 who have a high risk for progression to active disease, complete treatment is important

Liver Disease

- Rifampin for 4 months or the 12-dose INH + rifapentine regimen have several fold lower risk of hepatotoxicity and are preferred for patients with baseline liver disease or risk of hepatotoxicity
- For those with ALT > 2 to 3 times the ULN, chronic alcohol consumption, or severe liver disease manifested by low albumin, coagulopathy, or encephalopathy, the risks of treating TB infection may outweigh benefits. If TB infection treatment is undertaken, close monitoring is indicated
- When there is an indication for TB infection treatment in patients with advanced liver disease, such as, plans for liver transplantation, TB infection treatment should be conducted with advice of a TB or liver disease expert

County of Los Angeles Public Health

Choice of Treatment Regimen for TB infection — *continued*

HIV

- Persons living with HIV are a priority group for treatment of TB infection because of a substantially elevated risk for progression
- Drug interactions might complicate use of a rifamycin-containing regimen. Rifabutin in place of rifampin for 4 months may be an option to avoid certain drug interactions
- Treatment should be pursued with consultation with an HIV TB expert

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines

Immunosuppression (current or planned)

- Immunosuppressed persons are a priority group for treatment of TB infection because of elevated risk for progression
- Organ transplant recipient, treated with TNF-alpha antagonist (e.g., infliximab, etanercept, others)
- Steroids (equivalent of prednisone ≥15 mg/day for ≥1 month) or other immunosuppressive medications (e.g., cytotoxic chemotherapy)
- Drug-drug interactions, particularly with rifampin, might complicate TB infection treatment and may require additional monitoring
- For persons with planned immunosuppression, complete TB infection treatment prior to immunosuppressant administration. If this is not feasible, at least one month of TB infection treatment should be completed before immunosuppressant administration

Pregnancy and Breastfeeding

- Pregnancy is not a risk factor for progression of TB infection to active TB disease
- Pregnant women with a positive test for TB infection and a risk for rapid progression (e.g., HIV-positive, recent TB exposure and conversion to positive TST/IGRA) should be considered for initiation of TB infection treatment while pregnant.
- For women not at risk for rapid progression, TB infection treatment can be delayed until at least 3-6 months post-partum
- Both INH and rifampin are considered safe in pregnancy. The INH + rifapentine regimen has not been studied in pregnancy and should be avoided
- INH and rifamycins are found in breast milk in small quantities but are considered safe
- Exclusively breastfed infants and their mothers treated with INH should receive pyridoxine (B6) supplementation

Contact to multidrug-resistant TB (MDR-TB)

Treatment of persons with TB infection who are exposed to an infectious case of MDR-TB should be offered a regimen selected based on the resistance pattern of the index case. Consultation with a clinician with MDR-TB expertise is essential.

Resources

Los Angeles County TB Control Program
http://www.publichealth.lacounty.gov/tb
213-745-0800

California Department of Public Health
Tuberculosis Control Branch (TBCB)
http://www.cdph.ca.gov/programs/tb/Pages/default.aspx
510-620-3000

California TB Controllers Association
http://www.ctca.org/
510-479-6139

Centers for Disease Control and Prevention
Division of Tuberculosis Elimination
http://www.cdc.gov/tb/
800-232-4636

Centers for Disease Control & Prevention, Latent Tuberculosis Infection: Guide for Primary Health Care Providers
http://www.cdc.gov/tb/publications/LTBI/treatment.htm

Curry International Tuberculosis Center
Warmline Consultation Service
http://www.currytbcenter.ucsf.edu/
877-390-6682 or 510-238-5100

Saukkonen et al. ATS hepatotoxicity statement
https://doi.org/10.1164/rccm.200510-1666ST